IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

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Applicant(s)	:	Daftary et al.
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Examiner	:	Gollamudi Kishore
Title	:	Non-Pegylated Long-Circulating Liposomes

Commissioner for Patents
P.O. Box 1450
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SUPPLEMENTAL AMENDMENT AND RESPONSE TO FINAL OFFICE ACTION

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Sir:

This is in response to the Final Office Action mailed November 5, 2009 ("Final Office Action"). Although a first response was filed within the three month time period to respond (filed on February 5, 2010), it is believed that a petition of a two month extension of time and fees for this extension are necessary for the filing of this supplemental response since the Examiner did not enter the claim amendments. Accordingly, a petition for a 2 month extension of time is hereby requested, and the Office is hereby authorized to charge Deposit Account 50-4254 for a two month extension of time.

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. (Currently Amended) A process for manufacture of long circulating non-pegylated liposomes comprising: dissolving one or more phospholipids and one or more sterols in a solvent or mixture of solvents;

wherein the one or more phospholipids is a saturated phosphatidylcholine selected from the group consisting of distearoyl phosphatidylcholine (DSPC), hydrogenated soya phosphatidyl-choline (HSPC) and mixtures thereof;

removing the solvent or mixture of solvents and adding an aqueous hydration media to the phospholipids and sterols; or adding an aqueous hydration media to the phospholipids and sterols in the solution; and removing the solvent or mixture of solvents;

wherein the aqueous hydration media comprises ammonium sulfate and sucrose and the amount of aqueous hydration media used is in the range of 10 to 35 ml for each mmole of phospholipid present to form long circulating non-pegylated liposomes; and

removing ammonium sulphate from extraliposomal hydration medium by dialysis~~, ultrafiltration or column chromatography~~ using a sucrose-histidine buffer solution.

2. (original) The process of claim 1 wherein the amount of aqueous hydration media used is 30 ml for each mmole of phospholipid in the lipid solution.

3. (Previously Presented) The process of manufacture of non-pegylated liposomes of claim 1 further comprising loading the liposomes with a therapeutic or diagnostic agent after removal of the ammonium sulphate from the extraliposomal hydration medium.

4. (original) The process of claim 3, wherein the therapeutic agent is an antineoplastic agent.

5. (original) The process of claim 4, wherein the antineoplastic agent is selected from the group consisting of Doxorubicin hydrochloride, Daunorubicin hydrochloride, and Epirubicin hydrochloride.

6. (original) The process of claim 5, wherein the antineoplastic agent is Doxorubicin hydrochloride.

7. (original) The process of claim 1, wherein the molar ratio of phospholipid to sterol is from about 1:0.1-1:2.

8. (previously presented) The process of claim 7, wherein the molar ratio of phospholipid to sterol is about 1:0.7.

9. (previously canceled).

10. (previously presented) The process of claim 1, wherein the concentration of ammonium sulfate in aqueous hydration media is not less than 125 mmoles/liter.

11. (previously canceled).

12. (previously presented) The process of claim 1, wherein the phospholipid has a minimum of sixteen carbons fatty acid chain.

13. (previously canceled).

14. (previously presented) The process of claim 1, wherein the phospholipid is distearoyl phosphatidylcholine (DSPC) and wherein the sterol is cholesterol.

15. (original) The process of claim 1, wherein the non-pegylated liposomes are successively extruded through series of filters having pore sizes from 0.4 μm to 0.05 μm for sizing.

16. (original) A liposome manufactured by the process of claim 1.

17. (original) The liposome of claim 16, wherein the phospholipid comprises distearoyl phosphatidylcholine (DSPC) and the sterol comprises cholesterol.

18. (original) The liposome of claim 16, wherein the non-pegylated liposome further comprises a therapeutic or diagnostic agent.

19. (original) The liposome of claim 18, wherein said therapeutic agent comprises an antineoplastic agent.

20. (original) The liposome of claim 19, wherein the antineoplastic agent is selected from the group consisting of Doxorubicin hydrochloride, Daunorubicin hydrochloride, and Epirubicin hydrochloride.

21. (original) The liposome of claim 20, wherein the antineoplastic agent is Doxorubicin hydrochloride.

22. (original) The liposome of claim 16, wherein the average size of liposome is 0.06 μm to 0.16 μm in diameter.

23-62. (previously canceled).

63. (Previously Presented) A process for manufacture of non-pegylated liposomes comprising:

forming a lipid film by evaporating a solvent from a lipid solution comprising one or more phospholipids, a sterol, and a solvent; and

hydrating the lipid film by adding an aqueous hydration media to form a non-pegylated liposomal composition; wherein the aqueous hydration media comprises ammonium sulfate and sucrose and wherein the amount of aqueous hydration media used is in the range of 10 to 35 ml for each mmole of phospholipid present in the lipid solution; and

removing ammonium sulphate from extraliposomal hydration medium using a sucrose-histidine buffer solution.

64. (Previously Presented) The process of Claim 63 wherein the aqueous hydration media comprises greater than 125 mM ammonium sulfate and 100 mM to 500mM sucrose.

65. (Previously Presented) The process of Claim 63 wherein the aqueous hydration media comprises greater than 125 mM ammonium sulfate and 250 mM to 300 mM sucrose.

66. (Previously Presented) The process of Claim 63 wherein the amount of histidine in the sucrose-histidine buffer is 1 mM to 100 mM.

67. (Previously Presented) The process of Claim 63 wherein amount of histidine in the sucrose-histidine buffer is 8 to 12 mM.

68. (Previously Presented) The process of Claim 63 wherein amount of histidine in the sucrose-histidine buffer is 10 mM.

69. (Currently Amended) The ~~proces~~ process of Claim 1 wherein the long circulating non-pegylated liposomes have a blood circulation half life of at least 25 times longer than conventional non-liposomal formulations when tested in Swiss albino mice at equivalent doses.